PRESCRIBING INFORMATION: For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

MENOTAS HP 75

(MENOTROPHIN FOR INJECTION BP 75 IU)

COMPOSITION

Combipack of
A. Menotrophin for Injection BP 75 IU/Vial
Each vial contains:
Menotrophin BP equivalent to activity of
Luteinising Hormone.....75 IU
Follicle Stimulating Hormone.....75 IU
Excipients...Q.S.

B. Sodium Chloride Injection BP 0.9% w/v; 1 ml Ampoule
Each ml contains:
Sodium Chloride BP ..... 0.9% w/v
Water for Injection BP..... Q.S.

Reconstitute with 1 ml of Sodium Chloride Injection BP (0.9% w/v) provided in this pack.

DESCRIPTION

Menotas HP is a preparation of gonadotrophins, extracted from the urine of postmenopausal women. It contains follicle stimulating hormone (FSH) and luteinizing hormone (LH) in a ratio 1:1.

CLINICAL PHARMACOLOGY

Female: Menotrophin for injection, produces ovarian follicular growth and maturation in women who do not have primary ovarian failure. In order to produce final follicular maturation and ovulation in the absence of an endogenous LH surge, hCG must be administered following Menotrophin treatment, at a time when patient monitoring indicates sufficient follicular development has occurred.
Male: In the testes, Menotrophin for injection induces the maturation of the sertoli cells and the development of the spermatozoa. However, a high concentration of androgens within the testes is necessary and can be attained by a prior treatment using human chorionic gonadotrophins (hCG).
Human tissue or organ distribution of FSH and LH has not been studied for Menotrophin. Metabolism of FSH and LH has not been studied for Menotrophin in humans.

INDICATIONS

Women:
- Anovulation, including polycystic ovarian disease (PCOD), in women who have been unresponsive to treatment with clomiphene citrate.
- Controlled ovarian hyperstimulation to induce the development of multiple follicles for assisted reproductive technologies (ART)

Selection of Patients

1. A thorough gynecologic and endocrinologic evaluation, including an assessment of pelvic anatomy must be performed before treatment with Menotrophin. Patients with tubal obstruction should receive Menotrophin only if enrolled in an IVF program.
2. Primary ovarian failure should be excluded by the determination of gonadotrophin levels.
3. Careful examination should be made to rule out the presence of an early pregnancy.
4. Patients in late reproductive life have a greater predilection to endometrial carcinoma as well as a higher incidence of anovulatory disorders. A thorough diagnostic evaluation should always be performed in patients who demonstrate abnormal uterine bleeding or other signs of endometrial abnormalities before starting Menotrophin therapy.
5. Evaluation of the partner's fertility potential should be included in the workup.

Men:
Hypogonadotrophic hypogonadism in men: Menotrophin with concomitant human chorionic gonadotrophins therapy is indicated for the stimulation of spermatogenesis in men who have primary or secondary hypogonadotrophic hypogonadism.

DOSAGE AND ADMINISTRATION

Dosage

Anovulatory infertility:
The dosage and schedule of treatment must be determined according to the needs of each patient. Response is monitored by studying the patient's serum estradiol levels and vaginal ultrasound visualization of follicles. Menotrophin for injection may be given daily which should be maintained for 7 days by subcutaneous or intramuscular injection to provide a dose of 75 to 150 IU/day, and gradually adjusted if necessary until an adequate response is achieved, followed after 1 day by human chorionic gonadotrophins. In menstruating patients, treatment should be started on the 4th/5th day of the menstrual cycle. The treatment course should be abandoned if no response is seen. Once adequate follicular development is evident, administration of Menotrophin is stopped, and ovulation may then be induced by administering human chorionic gonadotrophins (hCG) at a dose of 5000 -10000 IU. The administration of hCG must be withheld in cases where the ovaries are abnormally enlarged on the last day of therapy. This should reduce the chance of developing ovarian hyperstimulation syndrome (OHSS).

Assisted Reproductive Technologies
The recommended initial dose of Menotrophin for injection for patients who have received a GnRH agonist for pituitary suppression is 150 to 300 IU/day. Based on clinical monitoring (including serum estradiol levels and vaginal ultrasound results) subsequent dosing should be adjusted according to individual patient response. Adjustments in dose should not be made more frequently than once every two days and should not exceed 150 IU per adjustment. The maximum daily dose of Menotrophin for injection given should not exceed 450 IU.
Once adequate follicular development is evident, hCG should be administered to induce final follicular maturation in preparation for oocyte retrieval. The administration of hCG must be withheld in cases where the ovaries are abnormally enlarged on the last day of therapy.
This should reduce the chance of developing OHSS.

Hypogonadotrophic hypogonadism in men
Spermatogenesis is stimulated with chorionic gonadotrophins (1000 – 2000 IU two to three times a week) and then Menotrophin for injection is given in a dose of 75 or 150 IU two or three times weekly. Treatment should be continued for at least 3 or 4 months.

Administration
Reconstitute with 1 ml of Sodium Chloride Injection BP (0.9% w/v) provided in this pack and administer subcutaneously or intramuscularly immediately. Any unused reconstituted material should be discarded. Parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration, whenever solution and container permit.

CONTRAINDICATIONS

Men and Women
1. Tumours of the pituitary or hypothalamic glands
2. Hypersensitivity to the active substance or any of the excipients used in the formulation

Women who have:
1. A high FSH level indicating primary ovarian failure.
2. Uncontrolled thyroid and adrenal dysfunction.
3. An organic intracranial lesion such as a pituitary tumor.
4. Sex hormone dependent tumors of the reproductive tract and accessory organs.
5. Abnormal uterine bleeding of undetermined origin.
6. Ovarian cysts or enlargement not due to polycystic ovary syndrome.
7. Menotrophin for injection is not indicated in women who are pregnant. There are limited human data on the effects of Menotrophin when administered during pregnancy.

Men
1. Tumours in the testes
2. Patients primary testicular failure are usually unresponsive to Menotrophin and hCG therapy.
3. Prostate carcinoma

WARNINGS AND PRECAUTIONS

Menotrophin for injection is a drug that should only be used by physicians who are thoroughly familiar with infertility problems. It is a potent gonadotrophic substance capable of Ovarian Hyperstimulation Syndrome (OHSS) in women with or without pulmonary or vascular complications. Gonadotrophin therapy requires a certain time commitment by physicians and supportive health professionals, and its use requires the availability of appropriate monitoring facilities.

Overstimulation of the ovary during Menotrophin therapy

Ovarian Enlargement: Mild to moderate uncomplicated ovarian enlargement which may be accompanied by abdominal distension and/or abdominal pain occurs in approximately 5 to 10 % of women treated with Menotrophin and hCG, and generally regresses without treatment within two or three weeks. The lowest dose consistent with expectation of good results and careful monitoring of ovarian response can further minimize the risk of overstimulation.

If the ovaries are abnormally enlarged or the serum estradiol concentration is excessively elevated on the last day of Menotrophin for injection therapy, hCG should not be administered in this course of treatment; this will reduce the chances of development of the Ovarian Hyperstimulation Syndrome (OHSS). In the event of hyperstimulation, the patient should refrain from sexual intercourse or to use barrier contraception methods for at least 4 days.

OHSS: OHSS is a medical event distinct from uncomplicated ovarian enlargement. OHSS may progress rapidly to become a serious medical event. It is characterized by an apparent dramatic increase in vascular permeability which can result in a rapid accumulation of fluid in the peritoneal cavity, thorax, and potentially, the pericardium. The early warning signs of development of OHSS are severe pelvic pain, nausea, vomiting, and weight gain.The following symptomatology has been seen with cases of OHSS: abdominal pain, abdominal distension, gastrointestinal symptoms including nausea, vomiting and diarrhea, severe ovarian enlargement, weight gain, dyspnea, and oliguria. Clinical evaluation may reveal hypovolemia, hemoconcentration, electrolyte imbalances, ascites, hemoperitoneum, pleural effusions, hydrothorax, acute pulmonary distress, and thromboembolic events.

Transient liver function test abnormalities suggestive of hepatic dysfunction, which may be accompanied by morphologic changes on liver biopsy, have been reported in association with the OHSS.

A physician experienced in the management of the syndrome, or who is experienced in the management of fluid and electrolyte imbalances, should be consulted.

Pulmonary and Vascular Complications

Serious pulmonary conditions (e.g. atelectasis, acute respiratory distress syndrome) have been reported. In addition, thromboembolic events both in association with, and separate from, the OHSS have been reported following Menotrophin therapy. In women with generally recognised risk factors for thromboembolic events, such as personal or family history, treatment with gonadotrophins may further increase the risk.

Multiple Pregnancies

The patient and her partner should be advised of the potential risk of multiple births before starting treatment.

Pregnancy wastage: Pregnancy wastage by miscarriage is higher in patients undergoing stimulation of follicular growth for ART procedures than in the normal population. The prevalence of congenital malformations after ART may be slightly higher than after spontaneous conceptions. This is thought to be due to differences in parental characteristics (e.g. maternal age, sperm characteristics) and multiple pregnancies.

PRECAUTIONS

General

Careful attention should be given to the diagnosis of infertility in the selection of candidates for Menotrophin therapy.

Laboratory Tests

The combination of both estradiol levels and ultrasonography are useful for monitoring the growth and development of follicles, timing hCG administration, as well as minimizing the risk of the OHSS and multiple gestations.

The clinical confirmation of ovulation, is determined by:

a. A rise in basal body temperature;

b. Increase in serum progesterone; and

c. Menstruation following the shift in basal body temperature. When used in conjunction with indices of progesterone production, sonographic visualization of the ovaries will assist in determining if ovulation has occurred. Sonographic evidence of ovulation may include the following:

a. Fluid in the cul-de-sac;

b. Ovarian stigmata

c. Collapsed follicle

Because of the subjectivity of the various tests for the determination of follicular maturation and ovulation, it cannot be overemphasized that the physician should choose tests with which he/she is thoroughly familiar. Interaction with other medicinal products and other forms of interaction No drug/drug interaction studies have been conducted with Menotrophin in humans. Pregnancy and lactation Menotrophin should not be given during pregnancy. It is Pregnancy Category X drug. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised if Menotrophin are administered to a nursing woman. Carcinogenesis and Mutagenesis Long-term toxicity studies in animals have not been performed to evaluate the carcinogenic potential of Menotrophin

ADVERSE REACTIONS:

The adverse events occurring at an incidence of >2% in women treated with Menotrophin are listed as below.

Body as a whole: Abdomen enlarged, Abdominal cramps, Abdominal fullness, Abdominal pain, Headache, Injection site pain, Injection site reaction, Malaise, Pain.

Digestive: Constipation, Diarrhea, Nausea, Vomiting.

Nervous System: Dizziness

Respiratory: dysponea

Urogenital: Breast tenderness, Hot flash, OHSS, Pelvic discomfort, Post retrieval pain.

Very rare cases of allergic reactions, localised or generalised, and hypersensitivity have been reported after treatment with gonadotrophin containing products

STORAGE

Store between 2°C-8°C.

Keep out of the sight and reach of children.

Keep the container in the outer carton in order to protect from light.

Do not refrigerate or Freeze.

PRESENTATION

Each box of MENOTAS HP 75 contains one Vial of sterile freeze-dried Menotrophin 75 IU & one ampoule containing 1 ml of Sodium Chloride Injection BP (0.9% w/v) as solvent.

USE IMMEDIATELY AFTER RECONSTITUTION.

Discard unused portion.

Manufactured by:

INTAS

INTAS PHARMACEUTICALS LTD.

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